PREVALENCE OF HELICOBACTER PYLORI IN GASTRIC FLUID IN THE SURGICAL PATIENT

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Department of Defense

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ABSTRACT

Helicobacter pylori is a bacterium that infects the human gastric mucosa. It is well established as a primary factor in peptic ulcer disease and has been implicated in the pathogenesis of gastric adenocarcinoma. Surveys consistently show that one half of the world s population carry *H. pylori*. *H. pylori* associated peptic ulcer disease afflicts approximately 10% of the U.S. population at some point during their lives. Once established, most infections last for decades and rarely resolve spontaneously. In this descriptive study gastric fluid was collected from 60 asymptomatic patients about to undergo general anesthesia. Gastric fluid was obtained and cultured to determine the presence of *H. pylori*. Ten percent cultured positive for the presence of *H. pylori*. Data analysis included descriptive and inferential statistics. Results indicated that culturing gastric juice for *H. pylori* is a simple, sensitive, and specific method to establish its presence and that nasogastric aspirates and tubes should be considered as potentially infectious. The observed 10% positivity for *H. pylori* within a group of 60 randomly selected military beneficiaries provides insight into the U.S. military population. The prevalence of *H. pylori* amongst military members is particularly interesting. The highly mobile nature and frequent travel puts the American soldier at increased risk for acquisition of this infection. Nurse practitioners are especially well suited to provide early diagnosis and treatment of infections such as *H. pylori* while implementing health maintenance and promotion efforts in order to decrease susceptibility. This novel approach to obtaining cultures for *H. pylori* is a cost effective and practical alternative for establishing the presence of this infection. In addition, knowing the prevalence of *H. pylori* among patients receiving care at military facilities will help guide nursing practice in early detection, treatment and prevention of this prevalent and costly infectious disease.

Key words: Adenocarcinoma, Dyspepsia, Gastritis, Helicobacter pylori, Peptic Ulcer Disease

PREVALENCE OF HELICOBACTER PYLORI IN GASTRIC FLUID IN THE SURGICAL PATIENT

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THESIS

Presented to the Graduate School of Nursing Faculty of

the Uniformed Services University of the Health Sciences

in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE DEGREE

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

May 1998

PREFACE

Before I was accepted into the Nurse Practitioner program I had some trepidation over the challenge of conducting a thesis project. When I entered the Graduate School of Nursing and was introduced to the faculty and their approach in helping the students become part of a well planned and supportive nursing research environment I was gladly relieved and my trepidation quickly dissipated. Right from the start I met encouragement and support. My research committee chairman, Dr. Monaghan, along with Dr. McMullen and Dr. Levine provided me with valuable guidance and respect. Their positive attitudes, ease of communication, and pleasant demeanor offered a nurturing setting for this novice researcher. Shortly, after starting down the research road I was introduced to Dr. Andre Dubois, Research Professor and Chief of the Laboratory of Gastrointestinal and Liver Studies. Dr. Dubois from our first meeting became a mentor of unending enthusiasm and a champion for my research project. His depth of knowledge and years of research related to *Helicobacter pylori* did not overshadow his willingness to welcome me into his laboratory and provide me with an open door to listen and edify. I owe a special thanks to Dr. J. Mysore for his technical expertise and patience in showing me the methods for culture and isolation of the bacterium. Family nurse practitioners are a new entity for the Air Force and the Uniformed Services University. The quality of education that the school provides and the environment of collaboration shared between the disciplines will allow nursing research to attain new heights and lead to further contributions by uniformed nurse practitioner researchers in the future.

DEDICATION

To Joanie for her love, support and joy that she brings to my life.

To Ciara and Trevor, my beautiful children, my most valuable gift.

To my parents Thomas and Hannah McManus for their love and unending support.

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CHAPTER ONE - INTRODUCTION

Helicobacter pylori is well established as a primary causative factor in peptic ulcer disease and has been defined by the World Health Organization as a carcinogen (International Agency for Research on Cancer, 1994). This bacterium is considered a pathogen because its presence is always associated with chronic active gastritis, and eradication of the bacterium is always followed by resolution of the gastritis. In addition, nearly all patients with duodenal ulcer disease have *H. pylori* gastritis, and ulcer relapse is exceptional after *H. pylori* eradication (Dubois, 1995). *Helicobacter pylori* infection has also been associated with persistent diarrhea and increased susceptibility to other infectious diseases (Clemens et al. 1995). Once established, most infections last for decades and rarely cure spontaneously, although they usually can be eradicated by antimicrobial therapy.

Surveys consistently show that approximately one half of the world s population carry *H. pylori*. *H. pylori* associated peptic ulcer disease afflicts approximately 10% of the U.S. population at some point during their lives and costs billions of dollars per year in physician fees and medications (Soll, 1993; National Institute of Health Consensus Development Panel on *Helicobacter pylori* in Peptic Ulcer Disease Conference [NIH], 1994). In the U.S. and western Europe, children rarely become infected, but more than half of all 60-year-olds have the bacteria. In contrast, 60 to 70 percent of the children in developing countries show positive test results by age 10, and the infection rate is even higher in adults.

The mode of transmission for this infection is not known. Direct interindividual transmission and/or consumption of food or water contaminated by saliva, gastric

contents, or feces may be a major factor (Ferguson et al. 1993; Thomas, Gibson, Darboe, Dale, & Weaver 1992; Young et al. 1996). In a study of 934 U.S. Army recruits, Smoak observed the prevalence of *H. pylori* to be 26.3% (Smoak, Kelly, & Taylor, 1994). In addition, Vaira and Hammermeister found that select subgroups of military members are at particularly high risk for the presence of *H. pylori* (Hammermeister et al. 1992; Vaira et al. 1991). Knowing the prevalence of *H. pylori* among the members eligible for military health care will help guide practice in early detection, treatment, and prevention, enabling our beneficiaries, active duty, retirees and dependents, to be at optimal health by decreasing the risk of infection.

The discovery of *H. pylori* has changed our concept of peptic ulcer disease from an acid related releasing condition to one where we can change the course of the disease. The presence of *H. pylori* was first seen as early as the late 19th century in animals and later at the turn of the 20th century in humans, (Dubois, 1995). At the onset of the 20th century, stress and dietary factors were believed to be related to the pathogenesis of peptic ulcer disease. The treatment at that time focused on hospitalization, bed rest and special diets consisting of bland foods. Further theories developed, focusing on digestive secretions such as gastric acid and their malevolent effects as pathogenic factors in the development of peptic ulcer disease. As a result antacids became the standard of therapy. Still later, in 1971, Sir James Black described the histamine H_2 receptor that seemed to the causative link in the production of gastric acid. Histamine receptor antagonists were developed which have proven to be safe and effective in the treatment of peptic ulcer disease. Recently, proton pump inhibitors have been shown to be highly effective as acid-suppressants and as antiulcer therapy (NIH, 1994).

Despite these sophisticated therapeutic agents, the disturbing problem of the high recurrence rate of peptic ulcer continues, even after complete healing has occurred. (NIH, 1994) It was not until 1983, that Marshall and Warren isolated this then unidentified curved bacilli in the gastric epithelium of patients with active chronic gastritis. Even then, it took almost 10 years for the medical community to be convinced of the evidence of a link between a bacterium and gastrointestinal disease (Marshall and Warren, 1983). Although their findings seem conclusive, Marshall and Warren s theory was hotly debated and remained in dispute. The debate continued even after Marshall and a colleague performed an experiment in which they infected themselves with *H. pylori* and developed gastritis (Marshall, 1996).

Microbiology

The organism was initially named Campylobacter Like Organism (CLO), but later studies revealed that it did not belong to the genus Campylobacter, and it was renamed *Helicobacter pylori* (Blaser, 1996).

Helicobacter pylori, a microaerophilic bacterium found primarily in the gastric antrum of humans, appears to be the most common infection worldwide (Soll, 1993, p.584). This gram negative bacterium has a curved, spiral, or gull-wing shape. It is 2.5 to 3.5 mm long and 0.5 to 1.0 mm in diameter with a periodicity of 1 to 2 mm. Its outer surfaces are smooth with one to six polar-sheathed flagella emerging from one of its rounded ends, making it highly motile (Dubois, 1995). It is microaerophilic and, as such, it grows best at oxygen levels of five percent. This percentage closely matches the oxygen level found in the stomach s mucous layer. It has an electropositive internal milieu which

helps it to fend off the onslaught of protons in the surrounding medium (Doolittle, 1997). Its survival in acid conditions depends, in part, on its ability to establish a positive inside-membrane potential in low pH (Tomb et al. 1997). *Helicobacter pylori* produces significant amounts of urease which cleaves urea into ammonia and carbon dioxide. The presence of urease is one of the biochemical markers used to help identify the presence of *H. pylori.* (Blaser, 1996).

Helicobacter is a genus composed of at least fifteen species (Table 1) which share common properties and characteristics. These properties provide the mechanisms that allow it to survive in the stomach, an ecological niche previously thought to be too inhibiting for bacteria to endure (Megraud, 1994). The criterion commonly used to justify positioning these animal isolates is the sequencing pattern of their ribosomal RNA, the 16S rRNA gene. This gene is a component of the ribosome which is essential for protein synthesis, (Lee, 1995, p. 615). Sequencing determines the similarity and relatedness, between bacteria. Bacteria are considered close relatives if their rRNA patterns are similar and they can be placed in the same genus if more than 90% of their patterns match. The different species are thought to have evolved from a common organism that adapted to inhabit the primordial stomach many years ago (Lee, 1995).

Table 1

Species of the Genus Helicobacter

Species	Hosts	Site
H. pylori[1]	Human, Rhesus monkey	Stomach
H. heilmannii[2]	Human, dog, cat	Stomach
H. rappini[3]	Human, sheep	Stomach, liver
H. pullorum[1]	Human, chicken	Stomach
H. felis [1]	Cat, dog	Stomach
H. acinonyx[1]	Cheetah	Stomach
H. mustelae[1]	Ferret	Stomach
H. nemestrinae[1]	Macaca nemestrina	Stomach
H. canis[1]	Human, dog	Intestine
H. cinaedi[1]	Human, hamster	Intestine
H. fennelliae[1]	Human	Intestine
H. muridarum[1]	Mice, rat	Intestine
H. pametensis[1]	Wild bird, pig	
H. bilis[1]	Mice (Inbred)	Intestine, liver
H. hepaticus[1]	Mice	Liver

Note. Adapted from Czinn, 1994; Megraud, 1994; Owen, 1995

Epidemiology

Helicobacter pylori infection of the stomach is the most frequent chronic infection in the world (McGuigan, 1996). Within the United States there are marked regional differences in the prevalence of *H. pylori* infection. The Incidence of infection is highest in populations in northeastern United States. The Midwest has a moderate incidence of infection, and the South and West have the lowest incidence (Parsonnet, 1992).

Information about *H. pylori* is evolving. The following summarizes what is known:

- *Helicobacter pylori* prevalence increases with age

- The infection is more prevalent in lower socioeconomic groups
- Crowded living conditions, such as institutions, increases the incidence and prevalence of this infection
- When socioeconomic factors are controlled for, African Americans and Hispanics have higher infection rates than Caucasians
- More than 50% of cases are acquired in childhood and adolescence
- The risk and rate of acquisition is highest in early childhood, after which the rate exponentially declines (Sipponen, 1997)
- Human-human transmission occurs often. In Canadian and American families, the mother and siblings of an infected child have a 75-80% risk of being infected. The risk in the general population is about 20%
- Infection rates are extremely high in Saudi Arabia, Asia, Albania, parts of Africa, and South America. In most developing countries, the majority of the population is infected by early adulthood (Cerda, Go, Loeb, & Westblom, 1994)

Transmission & Mechanism of Survival

The mode of transmission remains unknown, although either an oral-oral or a fecal-oral route is likely, so far studies have not been conclusive (Vaira et al. 1991). An interesting study reported by Moshopoulos and Skandalis (1996), examined sixty-four patients with duodenal ulcers and found 78% of the spouses of patients (N=42) positive for *H. pylori* were positive as well. Compared with 20% for the partners of the *H. pylori*

negative group(N=10), suggesting person to person transmission within couples or exposure to a common source of infection.

How *H. pylori* survives and acts on the stomach has been a matter of intense research. In the human stomach copious amounts of hydrochloric acid are produced and the pH is maintained at <2. Most bacteria cannot survive in such a low pH. When *H. pylori* enters the gastric lumen it is immersed in acidic gastric juice where small amounts of urea are present. *Helicobacter pylori* produces urease which breaks down the urea and produces ammonia. The ammonia, which elevates the pH, is produced in a cloud around the bacterium. This helps to protect the organism from the harsh acidic environment. Once in the stomach *H. pylori* embeds itself in the mucous layer that covers the gastric cell surface (Lee & Mitchell, 1994). The pH at the gastric epithelial cell surface is believed to be neutral. Urease activity, at this level, may still be an important factor in continued long-term survival by enabling the bacterium to utilize urea as a nitrogen source (Owen, 1995, p.428).

Almost 80% *H. pylori* live in the mucus layer of the infected hosts, while approximately 20% adhere to the mucosal epithelial cells using adherence pedestals (Owen, 1995). These adhesion pedestals, in turn, may attract neutrophils and generate an antibody response. It is this local inflammatory reaction that is thought to nourish the bacterium. Different strains produce different cytotoxins which, along with the urease produced, may contribute to the mucolytic changes that occur (Soll, 1993). Two phenotypic traits are characteristic of nearly all strains from persons with peptic ulcer disease or gastric cancer and are missing from many of the strains from asymptomatic carriers. The first is called VacA, a cytotoxin that produces prominent vacuoles in

cultured eukaryotic cells. The second is a large protein called CagA, a protein that is produced by most toxigenic strains, and not produced by most non-toxigenic strains. (Covacci et al. 1993: Cover, Dooley, & Blaser, 1992; Figura et al. 1989; Fox et al. 1992; Tummuru, Cover, & Blaser, 1993)

Clinical Syndrome

Helicobacter pylori contains and expresses an assortment of proinflammatory biomolecules. These biomolecules stimulate host cells to release proinflammatory substances which participate in the initiation and perpetuation of inflammation and tissue injury (McGuigan, 1996). The clinical syndrome of acute *Helicobacter* infection appears to be one of epigastric cramping pain, nausea, vomiting, flatulence, malaise. In some cases there may be a fever, and mucousy vomiting may also be present. The incubation period is from 1-7 days and may or may not be followed by a dyspeptic syndrome. These symptoms will last for about a week and then disappear, whether or not the organism has been spontaneously eliminated. The organism usually persists after initial infection, but may disappear spontaneously. There is an initial IgM response which declines, to be followed by IgG conversion; this persists unless the organism is partially or completely eradicated. (Axon, 1994)

Asymptomatic individuals may have many symptoms which remain hidden. The bacteria may have different virulence factors or host factors that may determine the consequences of infection (Axon, 1994). The prevalence of this infection in many populations is still unknown.

CHAPTER TWO - REVIEW OF LITERATURE

Civilian Populations

Staat and colleagues were the first to investigate *H. pylori* US population based prevalence. They demonstrated that even in developed countries, such as the USA, *H. pylori* is acquired in early life (Staat, Kruszon-Moran, McQuillan, & Kaslow, 1996). The team determined the prevalence of *H. pylori* infection in 2581 children between 6-19 years old by measuring anti-*H. pylori* IgG antibody concentrations. The researchers found that 24.8% of participants had evidence of Helicobacter infection. Infection was strongly associated with increasing age and ethnicity. Seventeen percent of non-Hispanic whites were infected, compared with 40% of non-Hispanic blacks, and 42% of Mexican Americans (Staat, 1996).

In the Staat study, the infection rate was higher among children from low-income families. The education level of the head of the household was also an important predictor of infection. Among Mexican Americans, birth outside the USA and Canada was an important independent risk factor for infection with *H. pylori* (Staat, 1996).

In Poland, Matysiak-Budnik et al. (1996) studied a group of 656 asymptomatic individuals ranging in age from 0-85 yrs. The overall rate of infection for all individuals was 73% versus 87% for those over the age of twenty. In addition there was an 18% seropositivity rate in those less than five years old as compared to 80% for those between the ages of 20 and 25. For the oldest group born between 1910 and 1970, the rate was between 80 and 100%. Ten percent of the Polish population has Peptic Ulcer disease and an incidence of gastric cancer on average of 36 per 100,000 inhabitants per year for men

(Matysiak-Budnik et al. 1996). This is of particular interest to US military members living or deployed to central Europe.

The highest rates of *H. pylori* infection occur in areas with the highest rates of stomach cancer, such as China, Japan, Peru and Scotland. However, even in the US, certain populations have higher rates of gastric cancer. In New Orleans, 70 percent of blacks are infected with *H. pylori*, and the gastric cancer rate in this population is 43 cases per 100,000 population. In whites living in New Orleans, the infection rate is about 43 percent, and the gastric cancer rate is 10 cases per 100,000 (Correa et al. 1990). In a recent report by Kennedy and Mahoney (1997), *H. pylori* was linked to sickle cell disease and recurrent abdominal pain in children. A new effort has begun to look at *H. pylori* in children and the effects of this infection on growth and development.

Uniformed Populations

Smoak and colleagues studied the seroprevalence of *H. pylori* infections in a cohort of US Army recruits (Smoak, Kelley, & Taylor, 1994). Sera were collected from a nationwide sample of 404 females and 534 males at induction into the US Army at Fort Jackson, South Carolina, during the fall of 1990. The purpose of the study was to determine the prevalence and examine risk factors of *H. pylori* infection in healthy young adults in the United States. The mean age of this group was 20.2 and the range was 17-26 years. Overall, this study found the *H. pylori* seropositivity rate in healthy young adults to be 20.8 percent. Age and ethnicity were strong predictive factors for *H. pylori* infection as well as living in an urbanized county of more than 1000 persons per square mile. Seropositivity rates nearly doubled from the youngest to the oldest age groups. Women of

all races had higher infection rates than did men. Among Hispanics, 52% of the females and 26% of the males were infected. The overall rate of positivity was 44% in blacks, 38% in Hispanics and 14% in whites (Smoak et al. 1994).

A study was done by Vaira and colleagues (1991) of 137 Italian soldiers living in a military barracks in Bologna, Italy. These soldiers were compared to 118 blood donors residing in the same country. The mean age of the soldiers was 20 years, similar to the blood donors mean age of 22.8. Forty six out of 137 (33.6%) of the soldiers had antibodies to *H. pylori* compared to thirteen of 118 (11%) of the blood donors. The soldiers had been living in the barracks for six months. The results indicate a higher prevalence of *H. pylori* antibodies in the military adults compared to the blood donors from the general population. The hypothesis that *H. pylori* infection is acquired by close personal contact between individuals is supported by this data.

Hyams et al. (1995) found almost a 2% yearly *H. pylori* seroconversion rate from a cohort study of 601 US military soldiers deployed for six months to South America, West Africa, the Mediterranean, or Saudi Arabia. This is approximately four times the rate for the general US population. This increased risk may result either from exposure to a high risk environment for *H. pylori* infection in enteric endemic areas or from crowding.

Hammermeister, et al. (1992) investigated the seroprevalence and incidence of *H. pylori* in submarine crews over a one year period. Sixty-four German submarine crew members were serologically compared to a group of fifty-four German Air Force staff. The results demonstrated a marked increase in seropositivity for the Submarine crews (39.1%), as compared to 18.9%. for the Air Force staff. The author concluded that

submarine crews serving their missions in an overcrowded space with extremely limited sanitary facilities must be considered a high-risk group for *H. pylori*.

CHAPTER THREE -CONCEPTUAL FRAMEWORK

The relevant theoretical perspective chosen for this study was derived from Akinsanya s model of bionursing. The purpose of this theory was to develop a link between nursing and the life sciences (anatomy, physiology, microbiology and pharmacology), separate from the traditional link through medicine (Akinsanya 1987b, Casey 1996). Akinsanya argues that since most disciplines which utilize knowledge from the biological sciences prefix their terms with bio (biomedical, biophysics, bioethics, etc), the use of the biological sciences in the teaching and practice of nursing should thus be termed bionursing. The direct link between bionursing and nursing care describes the impact that bionursing has on clinical practice by giving it the rationale for the tasks of nursing. It also examines the bioscience knowledge base required in the performance of required nursing tasks. This is where the bulk of Akinsanya s empirical work lies. He observed nursing activities and asked nurses what type of science knowledge they needed for the performance of those observed tasks (Akinsanya, 1987a). This thesis will draw directly from the knowledge of the sciences of microbiology , physiology, and pathophysiology. All of these branches of science will be brought together in unison at the completion of this bionursing research project.

Air Force family nurse practitioners will be utilized as health care providers throughout military facilities. As such, they will need to be kept up to date on new therapeutics, new techniques in patient management and areas of current research. Mastered prepared nurse practitioners will have the theoretical knowledge as well as the practical knowledge to assess research problems. They will be able to approach these problems from a firm foundation in the biological sciences. This will supply the health

care community with solid bionursing research that can be added to the scientific knowledge base of the medical community as a whole.

Nurse practitioners will also play a pivotal role in health maintenance and disease prevention. Epidemiological data obtained through research concerning different populations will support the diagnostic role of the nurse practitioner. Knowing the risk factors for *H. pylori* and being aware of current research in this area will help provide nurse practitioners with the knowledge to structure military environments in such a way as to diminish the risk of transmission of this infectious disease.

CHAPTER FOUR - METHODOLOGY

This research is a descriptive study designed to determine (1) whether gastric juice is a possible source of transmission of *H. pylori* and (2) the prevalence of *H. pylori* in surgical patients. It is an extension of a study conducted by K.A. Young and colleagues (1995) using a different population. Participants were patients who were scheduled to undergo surgery as part of their medical management and who were to receive a naso-gastric tube as part their care.

The participants consisted of a convenience sample from the 89th Medical Group, Malcolm Grow Medical Center, Andrews AFB. Institutional Review Board (IRB) approval was obtained from the Uniformed Services University of Health Sciences (USUHS) as well as from the 89th Medical Group Institutional Review Board. The study was desogned to utilize a sample size of 50 patients which was later extended to 60.

Study Population

Criteria for selection/inclusion:

The patients were greater than 18 years of age, hospitalized, scheduled to have surgery and were anticipated to receive a nasogastric or orogastric tube as part of their surgical management. There was no restriction for entry based on gender, physical or psychiatric condition other than the ability to give informed consent. A total of 60 patients were enrolled in the study over a six month period. The sample size was determined through power analysis using a small effect size of 0.34, a power of .80 and a level of significance of .05 (Burns, 1993).

Criteria for exclusion:

1. Inability to sign informed consent
2. Age less than 18 years
3. continuous tube feedings
4. Receiving one or more of the following medications

    Bismuth

    Clarithromycin

    Metronidazole

    Tetracycline

    Amoxicillin

    Proton pump inhibitors (i.e. Omeprazole)

Patients were selected by the investigator after consultation with the attending staff physician, thereby ensuring preservation of patients rights and avoiding any pressure to participate in the study. Patients received a coded research number which was used for sample identification to protect patient confidentiality.

After patients were identified as meeting the research criteria, the research protocol was explained and written consent obtained. Once informed consent was obtained, the patient received general anesthesia with subsequent placement of either a nasogastric or orogastric tube (GT). Upon confirmation of placement of the GT, 4 to 50 mL. of gastric fluid was aspirated using sterile techniques and a sterile 60 mL. catheter tip syringe. The fluid was then transferred to a sterile specimen tube where phenol red was added to the fluid until a yellow color appeared and then the pH was tested. Sodium

bicarbonate, 7.5%, was titrated to the sample until a pH of seven was obtained (red color). The fluid was sealed, placed on wet ice and later taken to the laboratory of Gastrointestinal and Liver Studies at USUHS for culture. A 200 uL aliquot of the fluid was streaked on Campylobacter chocolatized agar plate supplemented with trimethoprim, vancomycin, amphotericin B, and polymyxin B and incubated at 37•C in an atmosphere of 90% N_2, 5% O_2, and 5% CO_2. Presence of *H. pylori* was identified as forming pinhead-sized water spray colonies within 7-10 days, have urease, oxidase and catalase activities, and seen by microscopy as Gram-negative curved or gull wings rods. Gram stain morphology was confirmed by an expert in *H. pylori* research.

Data analysis includes predominantly the use of descriptive statistics to report the presence of *H. pylori* in the gastric fluid in this population. Additionally, demographic data allows for description of the sample and permits comparisons between groups based on demographic characteristics.

CHAPTER 5 - DATA ANALYSIS

After receiving approval from the Institutional Review Board (see Appendix A & B), gastric fluid was obtained from a convenience sample of patients following informed consent. These volunteers were pre-scheduled to have general anesthesia for surgery at a medium-sized military medical facility. Summary measures such as percentages were used to describe the sample.

Fresh gastric fluid samples were obtained from patients undergoing surgery for a variety of reasons. Participation was based on ability to understand and sign the consent form, age greater than eighteen, and no evidence of use of amoxicillin, clarithromycin, metronidazole, bismuth, or antisecretory agents within the last twenty-four hours. Once informed consent was obtained, the gastric fluid was aspirated, neutralized, sealed and placed on wet ice and later taken the laboratory for analysis.

When a subject was found to be positive, notification in the form of a letter, (Appendix L), was given to the subject s staff surgeon. In addition, if a participant requested to know their status, positive/negative, a phone call or letter was given to the participant with the culture results.

A total of sixty gastric fluid samples were obtained from the study subjects who consisted of 55% females and 45% males. The age range was nineteen to seventy-five years, with a mean age of thirthy-three. From the samples of gastric fluid 10% were determined to be positive for *H. pylori* by culture. There were eighteen active duty members and one of them was positive for *H. pylori.* The other positive participants were two dependents and three retirees.

A culture was defined as positive if:

1. Growth had the typical water-spray appearance
2. Colonies were positive for catalase, oxidase, and urease
3. Bacteria were Gram negative and had a curved rod morphology

The amount of gastric fluid obtained ranged from 2mL. to 50mL. The average amount of gastric juice aspirated was 16.5mL. For the six subjects that were positive the range of gastric fluid aspirated was 3mL. to 38mL., the average being 16.8mL. One-third of these samples were less than 10mL. This is in contrast to the findings of Young (1997), who found *H. pylori* positive fluid only in samples that were greater than 10mL.

Age

The average age of those infected was forty-four, with a range of twenty-seven to sixty-six (Table 2).

Table 2

Helicobacter pylori Positive or Negative by Age

Age	Positive for HP/Total (N)	Percent Positive
22-40	2/18	11%
41-60	3/25	12%
61-80	1/17	6%
Total	6/60	10%

Race

The ethnic background of the sample population was as follows: Thirty-nine (65%) were Caucasian, fifteen (25%) Afro-American, four (7%) Asian, and two (3%) were Hispanic. Of those that were positive three (50%) were Caucasian, two (33%) were African-American, and one (16%) was Hispanic. Two of the six (33%) that were positive for *H. pylori*, (one Hispanic, one Caucasian),were born outside of the United States.

Education

Seventy percent (45) of the sample population had completed high school. While fifteen (25%) had less than twelve years of schooling, five (8%) had greater than sixteen years of education. Among those who were *H. pylori* positive, five (83%) had completed high school but none had been to college.

Socioeconomic Status

Socioeconomic status was divided into three categories, those earning less than 50,000 dollars per year, $50,000 to $100,000 dollars per year, and those earning greater than $100,000 dollars per year. Fifty-three percent (32) earned less than $50,000 dollars per year, 38% (23) earned $50,000-$100,000 dollars per year, and eight percent (5) earned more than $100,000 per year. Among the six who were positive for *H. pylori* half (3) earned less then $50,000 dollars per year, one earned $50,000 to $100,000 per year and two earned more than $100,000 per year (Table 3).

Table 3

Annual Income of Study Subjects

Annual Income	Positive for HP/Total (N)	Percent Positive
Less than $50,000	3/32	9%
$50,000 - $100,000	1/23	4%
More than $100,000	2/5	40%
Total	6/60	10%

Crowding

Higher frequency of testing positive for *Helicobacter pylori* has been found in people living in crowded conditions (Dubois,1995). Sample population participants were asked how many people lived in their household before they reached the age of ten. For the sample population, 22% of the sample had a household size of ≥ 7 people while 5% had a household size was 3-6 people, (Table 4).

Table 4

Number of People Living in Household before Age Ten

Number	Positive for HP/Total (N)	Percent Positive
1-6	2/42	5%
7 or greater	4/18	22%
Total	6/60	10%

Limitations

Although sample size was ample for the scope and aim of this study, it is difficult to perform statistical analysis since only six subjects were found to be positive for *H. pylori*. Gastric fluid culture is a novel method for isolating *H. pylori* and the rate of positivity might have been enhanced with collection of either endoscopic gastric biopsies, serology or breath testing. The nature of the surgical patient with frequent pre-operative and/or recent use of antibiotics could have been a factor in the number of negative cultures; however it is important to note that none of the subjects positive for *H. pylori* received preoperative antibiotics while 11 of the *H. pylori* negative were treated with preoperative antibiotics. Other factors such as the position of the nasogastric tube and the possible dilutional effect of such pre-medications as Bicitra®, sodium bicarbonate, could also have contributed to a lower yield of positivity. However the pH of gastric juice sampled 1-3 hours after Bicitra® administration was not different from the pH in subjects who did not receive Bicitra®. The use of sodium bicarbonate could potentially have led to a rebound in acid production with subsequent lowering of the gastric pH. Although the gastric juice was immediately neutralized and placed on ice there was a delay of unknown duration between rebound acid secretion following Bicitra® administration

CHAPTER 6 - CONCLUSIONS

Prevalence of *H. pylori* infection increases with age and varies among racial groups in the United States. Approximately 10 percent of Caucasians below the age of 35 are infected with *H. pylori*, increasing by 10% for each subsequent decade of life. Prevalence is higher among African-Americans where 45 percent of those 25 years of age or less are infected (Damianos & McGarrity, 1997). The results of this experiment are in agreement with these epidemiological data. The observed 10% positivity for *H. pylori* within a group of 60 randomly selected patients undergoing general anesthesia for scheduled surgery, provides insight into the U.S. military population. This study confirms that for military surgical patients within the continental United States, the prevalence of *H. pylori* is similar to that of the population of the nation as a whole.

This study examined gastric fluid and found similar results than previous studies using gastric biopsy, the gold standard for determining the presence of *H. pylori*. Culturing gastric juice for *H. pylori* is a simple, sensitive and specific method to establish the presence of *H. pylori*. In an article that was published after this study was initiated, Mokuolu (1997) found similar results measuring gastric juice urease activity in 57 patients and finding gastric juice urease activity to be a reliable, inexpensive and readily available.

The prevalence of *H. pylori* amongst military members is particularly interesting. The highly mobile nature and frequent travel to often harsh environments puts the American soldier at particular risk for acquisition of this infection.

Nurse practitioners are particularly well suited to provide early diagnosis and treatment of infections such as *Helicobacter pylori* while implementing health maintenance and promotion efforts in order to decrease incidence of the infection. The term Bionursing

as envisioned by Askansazi is the incorporation and utilization of those core courses required for nursing education such as Physiology, Biochemistry, Pathophysiology and Microbiology in order to enhance the breath of knowledge of nurses while providing a broad scientific background leading to well-grounded nursing research. This study drew from these core disciplines and demonstrated an example of Bionursing research. These branches of science were brought together in unison at the completion of this study and have led to further questions as well as continued research by the investigator.

Nurse practitioners, nurse researchers, and other health providers armed with up to date epidemiological information related to areas of deployment as well as permanent foreign base sites are positioned at the forefront of the fight against infectious disease. Mastered prepared nurse practitioners have the theoretical knowledge as well as the practical knowledge to assess research problems, approaching such problems from a firm foundation in the biological sciences. In order to prevent such diseases as *H. pylori,* it is essential to clarify its epidemiology and mode of transmission. The results of this study demonstrate that nasogastric aspirates and tubes should be considered as potentially infectious

Research related to *H. pylori* has exploded after Warren and Marshall (1983) first reported a link between these curved microscopic organisms now called *H. pylori,* and chronic gastritis. Although nearly fifteen years have passed since that report, the research effort continues with great enthusiasm. Researchers are delving into every aspect of the nature, the mode of transmission, the genetic make-up, and the chemistry of *Helicobacter pylori* and its impact on humans.

Areas for Further Research

Helicobacter pylori provides for an exciting area of research. There are many unanswered questions related to mode of transmission, virulence, carcinogenicity and why some populations seem to be inherently predisposed to this infection. The recent sequencing of the *H. pylori* genome is sure to lead to further discoveries and to further questions. One of the benefits of the present study is that the *H. pylori* strains isolated from this population will be typed for the presence of virulence factor (*cagA*). This will provide insight into the type of bacteria present in a very special population that is not generally studied, and may represent the majority of uniformed personnel. Likewise, the effects of deployments and the close living arrangements that are often found while deployed offer an excellent opportunity for discovering some of the answers to this puzzling disease and potentially provide methods to prevent its transmission. Studies involving submariners, during long missions, as well as astronauts, on prolonged space flights, may provide good models for military personnel restricted to close quarters. Furthermore, conducting a study with a larger sample size at other military facilities using gastric fluid, sera, tissue samples or the newly FDA-approved breath test for *H. pylori* can be fertile ground for further research. Another area that is just beginning to be explored is the mode of transmission of *H. pylori* to children and its long term effects on growth and development; a particularly interesting area for Family Nurse Practitioners.

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LIST OF APPENDICES

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

May 14,1997

MEMORANDUM FOR TERENCE J. MCMANUS, GRADUATE SCHOOL OF NURSING

SUBJECT: IRB Approval for Protocol T06129-01 Involving Human Subject Use

The new protocol entitled ***"Prevalence of Helicobacter pylori in Gastric Fluid in the Surgical Patient"*** received an expedited review on 5/9/97 and was **APPROVED** by Edmund G. Howe, M.D., J.D., Chairperson, Institutional Review Board on 5/9/97. This protocol is considered to be not greater than minimal risk in accordance with 32 CFR 219.110 (8). This is a descriptive study to ascertain the incidence of Helicobacter pylori in surgical patients. Subjects will be randomly selected volunteers who are scheduled to have a surgical procedure where introduction of a nasogastric tube is anticipated. Up to fifteen ml of gastric fluid, normally discarded, will be removed from the patient's stomach through the nasogastric tube, frozen, and sent to USUHS for analysis. Approval from Malcolm Grow IRB where study will be conducted already received.

The consent form approved for use is attached. It is your responsibility to review and maintain an accurate and accessible file of all consent forms used in this study for each study site. This research study will be reviewed within one year of this date, unless otherwise completed.

Please notify this office of any amendments you wish to propose and of any adverse events which may occur in the conduct of this project. If you have any questions regarding human volunteers, please call me at 301-295-330

Michael J. McCreery, Ph.D.
LTC, MS, USA
Director, Research Programs and
Executive Secretary, IRB

Attachments:
A/S

DEPARTMENT OF THE AIR FORCE
HEADQUARTERS 89TH AIRLIFT WING (AMC)

U.S. AIR FORCE
1947 - 1997

18 Feb 97

MEMORANDUM FOR CAPTAIN TERRY McMANUS

FROM: 89 MDG/SGI

SUBJECT: Approval of Protocol: Prevalence of Helicobacter pylori in Gastric Fluid

1. The Institutional Review Board following both a technical and ethical review approved you protocol at its 12 Feb 97 meeting. You may begin your study.

2. Please ensure all required reports and copies of informed consent documents are forwarded to this office promptly.

ISADORE NEUROCK. DDS
Director of Medical Education

DEPARTMENT OF THE AIR FORCE
HEADQUARTERS 89TH AIRLIFT WING (AMC)

1947 - 1997

11 February 1997

MEMORANDUM FOR SGI

FROM: SGJ

SUBJECT: Research Protocol "Prevalence of Heiicobacter pylori in Gastric Fluid, Captain Terence J. McManus, USAF, NC

1. I have reviewed the above mentioned protocol and fmd the informed consent document does not require the witnesses SSN number. On page 2 of 3 of the informed consent para 12, please change the word "he" to "she".

2. I also recommend adding the following paragraph found in Chapter 3 of AFI 40-404 (Para 3.1.6.1.), "Any medical misadventure or unanticipated medical event will be brought immediately to the attention of the subject, or the subject's guardian or next of kin, if the subject is not competent at the time to understand the nature of the misadventure or unanticipated medical event."

3. Please add paragraphs (g) regarding the Privacy Act Statement - Health Care Records and (j) the voluntary participation statement of Attachment 4 of AFI 40-403.

4. After the above mentioned changes have been made this informed consent will comply with the requirements set out in AFI 40-403. I do not need to review the document once the modifications are made. I recommend its approval.

MARYALICE DAVID, Capt, USAF
Medical Law Consultant

Attachment
Protocol
Portions of AFI 40-403

25 Feb 97

MEMORANDUM TO: USUHS IRB
Att.: LtCol McCreery

SUBJECT: Funding for (Budget Request) USUHS Intramural Research Protocol

FROM: Capt Terry McManus

1. CONSUMABLE SUPPLIES:

   1. 80 Chocolatized Campy Blood Agar pIates at a cost $3.30 each for a total of $264, for the initial isolation of the ***Helicobacter pylori*** bacterium from the gastric fluid. ($264)

   2. 80 Blood Agar plates at a cost of $1.10 each for a total of $88, for the further isolation of the ***Helicobacter pylori*** bacterium. ($88)

   3. Chemicals, pipettes, reagents, gas for incubator, pH paper, and general laboratory supplies $350. ($350)

2. OTHER COSTS:

   Photocopying, paper, and computer costs for data entry $48. ($48)
   ($750)

   Total budget request $750.

3. Thank you for your consideration.

Terence J. McManus, Capt, USAF, NC
Family Nurse Practitioner Student
Graduate School of Nursing

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

July 29, 1997

MEMORANDUM FOR TERENCE J.McMANUS, GRADUATE SCHOOL OF NURSING

SUBJECT: Notice of Fund Approval (T06129-01)

Attached is the Notice of Fund Approval for the above referenced graduate nursing student project. Funds have been authorized as shown.

If you have any questions or concerns, please contact Michael P. Giza in the Office of Research at 295-9815.

Beth Bowden
Director, Grants Administration

Attachment
cc:
Dean, GSN

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

July 29, 1997

NOTICE OF FUND APPROVAL*
Change No.:Original

Project No: T06129-01
Principal Investigator: Terence J. McManus
Project Title: Prevalence of Helicobacter Pylori in Gastric Fluid in the Surgical Patient

Project Period: From 4/ 1/97 Through 9/30/97
Budget Period: From 4/ 1/97 Through 9/30/97

	TYPE OF EXPENSE	BUDGET
1.	Personnel Support	$0
2.	Supplies/Equipment/Other Expenses	$500
3.	Travel	$0
	TOTAL	$500

*Fund approval is contingent upon the appropriation of funds to USUHS. Travel (except that which is an approved part of the project) may not be charged to the project. Major equipment with unit cost equal to or greater that $5,000 will be charged against separate funds.

Funding Accomplished 4/24/97 Budget Officer Verna M. Hill

Questions regarding this award may be directed to the Office of Research

Ruth Ellen Bulger, Ph.D.
Vice President for Research

19 Sept 97

MEMORANDUM FOR Captain Terry McManus

FROM: 89 MDG/SGI

SUBJECT: Extension of Helicobacter Study

1. The Institutional Review Board (IRB) Committee approved the extension of the protocol "PREVALENCE OF HELICOBACTER PYLORI IN GASTRIC FLUID IN THE SURGICAL PATIENT" on 10 Sep 97.

2. Please ensure all progress and final reports are forwarded to my office promptly.

William H. Aussiker

WILLIAM H. AUSSIKER, Col, USAF, DC
Director, Career Development Function

CONSENT FORM

APPROVED FOR USE

DATE 7 MAY 1997

INITIALS

Date:

89th Medical Group
ANDREWS AFB, MARYLAND

Consent for Voluntary Participation in a Clinical Investigation Study

1. I, , have been asked to voluntary participate in a research project entitled, "Prevalence of *Helicobacter pylori* in Gastric Fluid in the Surgical Patient" being conducted at the 89th Medical Group, Andrews AFB, Maryland.

2. The procedure for this project involves: Analyzing gastric fluid that is normally discarded. Removing 10-15 mL. of this fluid from my stomach from a tube that will be in my nose, mouth or stomach. Removal of small amounts of gastric fluid is part of the normal nursing procedure for maintenance of these tubes. This tube will be already be in place related to my medical management and will not be placed specifically for this study. I understand that this procedure is not painful and will not have any effect on my medicaI or surgical condition.

3. The purpose of this research project is to: Determine the presence of the bacteria *Helicobacter pylori,* in stomach fluid in patients who have been admitted to an intensive care unit. *Helicobacter pylori* is an organism that has been found to be a factor in some forms of stomach inflamm ation and specific types of ulcers. Humans are at increased risk for becoming infected with this bacteria as they age. Many people are infected with this bacteria and have no symptoms. Many questions remain unanswered regarding this bacteria, such as how do people become infected, why do some people have symptoms while others do not, and where in the body can this bacteria be found.

4. A total of 50 subjects are expected to participate in this project.

5. The risks or discomforts during the removal of the stomach fluid include clogging of or unintentional removal of the tube.

6. I understand that the research may or may not help me personally but that the results may help the investigator learn about the prevalence of *Helicobacter pylori* in stomach fluid in patients admitted to an intensive care unit. It is expected that this information will lead to further research related to *Helicobacter pylori* prevalence and presence in gastric fluid. At this time the presence of *Helicobacter pylori* in patients who do not have symptoms is not an indicator for treatment to remove the bacteria. If at a later time, it is determined that I have peptic ulcer disease, the information regarding my *Helicobacter pylori* status will help the physician in the treatment of my condition.

7. I understand that I may withdraw from this study at any time without prejudice to my future care. I understand that if I withdraw from this project, I will not lose any benefits to which I am otherwise entitled.

8. I have been informed that there will be no additional costs to me beyond those normally associated with my care at the 89th Medical Group, Andrews AFB.

I understand and accept these risks. _____ Subject/Patient Initials

9. Any new significant finding developed during the course of the research which may effect my willingness to participate further will be explained to me.

10. In all publications and presentations resulting from this research project, my anonymity will be protected to the maximum extent possible; however, I realize that authorized Air Force Medical Department personnel may have access to my research file in order to verify that my rights have been safeguarded.

11. If I suffer any physical injury as a result of my participation in this study, immediate medical treatment is available at the 89th Medical Group, Andrews AFB, Maryland. I understand that although no compensation is available, any injury as a result of my participation will be evaluated and treated in keeping with the benefits or care to which I am entitled under applicable regulations.

12. Any medical misadventure or unanticipated medical event will be brought immediately to the attention of the subject, or the subject s guardian or next of kin, if the subject is not competent at the time to understand the nature of the misadventure or unanticipated medical event.

13. If I have any questions regarding this research project, I may contact Captain Terry McManus at 301-599-6554. If I have any questions regarding my rights as an individual while participating in a research project at the 89th Medical Group, Andrews AFB, I can contact the Medical Legal Consultant Captain David at (301) 981-4440. She will answer my questions or refer me to a member of the Committee for the Protection of Human Subjects for further information. If I believe I have been injured as a result of this project I may call the legal office (301) 295-2215.

14. I understand that my participation in this project is voluntary and that my refusal to participate will involve no penalty or loss of benefits to which I am entitled under applicable regulations. If I choose to participate, I am free to ask questions or to withdraw from the project at any time. If I should decide to withdraw from the research project, I will notify Captain Terry McManus at 301-599-6554, to ensure an orderly termination process. My withdrawal will not involve loss of benefits to which I am entitled.

I certify that I have received a copy of this consent form.

_____ _____
Date Signed Patient/Subject Signature

_____
Printed Name-Status-Sponsor's SSN

_____ _____
Witness' Signature & Date Investigator Signature & Date

_____ _____
Witness' printed Name Investigator printed Name-
Rank

PRIVACY ACT STATEMENTS

1. Authority. 5 USC 301

2. Purpose. Medical research information will be collected to enhance basic medical knowledge, or to develop tests, procedures, and equipment to improve the diagnosis, treatment, or prevention of illness, injury or performance impairment.

3. Use. Medical research information will be used for statistical analysis and reports by the Departments of the Air Force and Defense, and other U.S. Government agencies, provided this use is compatible with the purpose for which the information was collected. Use of the information may be granted to non-Government agencies or individuals by the Surgeon General in accordance with the provisions of the Freedom of Information Act.

4. Disclosure. I understand that all information contained in this Consent Statement or derived from the experiment described herein will be retained permanently at 89th Medical Group, Andrews AFB, Maryland and salient portions thereof may be entered into my health record. I voluntarily agree to its disclosure to agencies or individuals identified in the preceding paragraph and I have been informed that failure to agree to such disclosure may negate the purposes for which the experiment was conducted.

5. Records. Records of my participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C. 552a, and its implementing regulations. DD Form 2005, Privacy Act Statement--Health Care Records, contains the Privacy Act Statement for the records. I understand that records of the study may be inspected by the US Food and Drug Administration (FDA).

6. Voluntary Decision. The decision to participate in this study is completely voluntary on my part. No one has coerced or intimidated me into participating in this program . I am participating because I want to. Captain McManus has adequately answered any and all questions I have about this study, my participation, and the procedures involved. I understand that Captain McManus will be available to answer any questions concerning procedures throughout this study. I understand that if significant new findings develop during the course of this study which may relate to my decision to continue participation, I will be informed. I further understand that I may withdraw this consent at any time and discontinue further participation in this study without prejudice to my entitlements to care. I also understand that the investigator of this study may terminate my participation in this study if he or she feels this to be in my best interest.

Subject/Guardian Signature

_____

Date_____

Signature of Witness

_____

Date_____

Printed Name, Grade or Rank

_____

DATA COLLECTION

ID NUMBER _____

AMOUNT OF FLUID _____

SOURCE OF FLUID _____

AGE _____ SEX _____

RACE _____ COUNTRY OF BIRTH _____

OF INDIVIDUALS IN HOME FROM BIRTH TO 10 YRS _____

HOUSEHOLD INCOME < 50,000 _____ 50,000-100,000 _____ >100,000 _____

EDUCATIONAL LEVEL _____

DIAGNOSIS _____

PERTINENT MED. HX _____

MEDICATIONS _____

GROWTH AFTER 7 DAYS _____

GROWTH AFTER 10 DAYS _____

CATALASE Pos/Neg OXIDASE Pos/Neg UREASE Pos/Neg

GRAM STAIN _____

H. PYLORI: NEGATIVE _____ POSITIVE _____

J

September, ,1997

Dear Doctor,

My name is Captain Terry M cManus and I am a Nurse Practitioner Graduate Student at the Uniformed Services University of the Health Sciences, (USUHS). Over the last few months, I have been collecting gastric fluid samples under the 89th MDG & USUHS IRBs approved protocol T06129-01 (18 February 1997). This protocol has been performed as part of my Thesis entitled "The Prevalence of *Helicobacter pylori* in Gastric Fluid in the Surgical Patient".

On 1997, I collected a sample of gastric fluid from ,who was under your care for surgery. The cultures were grown at USUHS in the Gastrointestinal and Liver Studies Laboratory under the guidance of Dr. Andre Dubois MD, PhD. The cultures for this patient were positive for *Helicobacter pylori*. Although I thought it might be useful for you to know this result, I am sure you are aware that it is currently recommended to treat *H. pylori* infection only in patients with Peptic Ulcer Disease or Mucosa Associated Lymphoid Tissue (MALT) lymphoma. Patients who have no specific gastroduodenal complaints and are *H. pylori* positive should not be treated for this infection

If you have any questions, I can be reached at 301-599-6554 or via E-mail at TMCMANUS@AOL.COM.

Sincerely,

Captain Terence J. McManus, NC, USAF
Family Nurse Practitioner Student
Graduate School of Nursing
Uniformed Services University of the Health Sciences